

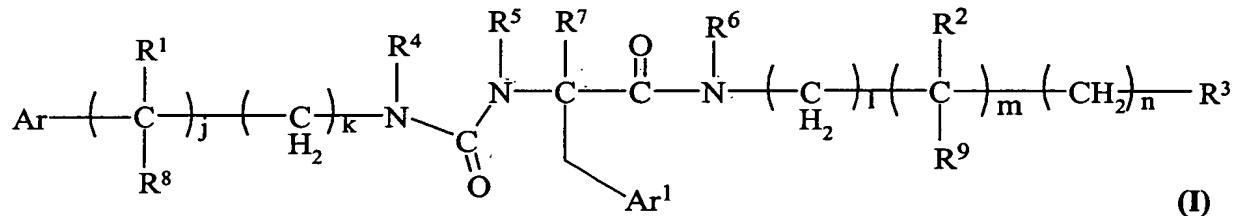
CLAIMS

5 1) A method for treating:

sexual dysfunctions, anxiety and panic disorders, social phobia, pulmonary hypertension, lung repair and lung development disorders, prostate cancer, pancreatic cancer, hepatic porphyria, visceral pain, gastrointestinal secretory disturbances, emesis or anorexia, inflammatory pain, neuropathic pain, cancer pain, postoperative pain, trigeminal neuralgia pain, acute herpetic pain and post herpetic pain,

10 *etc*

comprising administering to a subject suffering therefrom and in need of treatment an effective amount of a compound of Formula I



15 or a pharmaceutically acceptable salt thereof wherein

j is 0 or 1;

k is 0 or 1;

l is 0, 1, 2, or 3;

20 m is 0 or 1;

n is 0, 1 or 2;

Ar is phenyl, pyridyl or pyrimidyl, each unsubstituted or substituted by from 1 to 3 substituents selected from alkyl, halogen, alkoxy, acetyl, nitro, amino, $-\text{CH}_2\text{NR}^{10}\text{R}^{11}$, cyano, $-\text{CF}_3$, $-\text{NHCONH}_2$, and $-\text{CO}_2\text{R}^{12}$;

25 R^1 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms;

R^8 is hydrogen or forms a ring with R^1 of from 3 to 7 carbon atoms;

R^2 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 8 carbon atoms

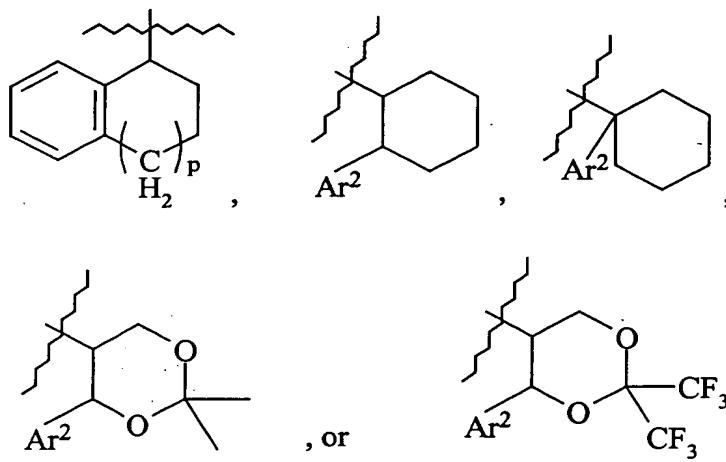
which can also contain 1 to 2 oxygen or nitrogen atoms;

R^9 is hydrogen or forms a ring of from 3 to 7 carbon atoms with R^2 which can contain an oxygen or nitrogen atom; or R^2 and R^9 can together be a carbonyl;

Ar^1 can be independently selected from Ar and can also include pyridyl-N-oxide, indolyl, imidazolyl, and pyridyl;

5 R^4 , R^5 , R^6 , and R^7 are each independently selected from hydrogen and lower alkyl; R^4 can also form with R^5 a covalent link of 2 to 3 atoms which may include an oxygen or a nitrogen atom;

10 R^3 can be independently selected from Ar or is hydrogen, hydroxy, $-NMe_2$, N -methyl-pyrrolyl, imidazolyl, N -methyl-imidazolyl, tetrazolyl, N -methyl-tetrazolyl, thiazolyl, $-CONR^{13}R^{14}$, alkoxy,

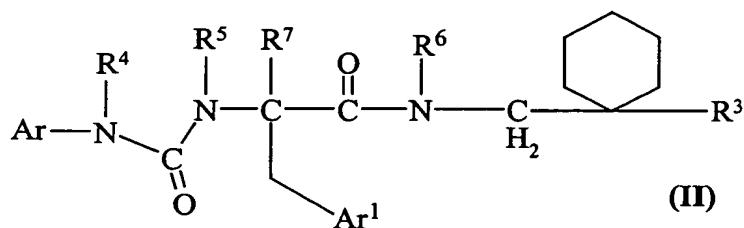


phenyl or pyridyl;

15 R^{10} , R^{11} , R^{12} , R^{13} and R^{14} are each independently selected from hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms.

15

2) A method according to Claim 1 employing a compound of Formula II



wherein

Ar is phenyl unsubstituted or substituted with 1 or 2 substituents selected from isopropyl, halo, nitro, and cyano;

R⁴, R⁵, and R⁶ are hydrogen;

R⁷ is methyl or hydrogen;

5 R³ is 2-pyridyl or hydroxy; and

Ar¹ is indolyl, pyridyl, pyridyl-N-oxide, or imidazolyl.

3) A method according to Claim 1 for treating female sexual dysfunctions.

10 4) A method according to Claim 1 for treating male sexual dysfunctions.

5) A method according to Claim 1 for treating anxiety, social phobia or panic disorders.

6) A method according to Claim 1 for treating pulmonary hypertension.

15 7) A method according to Claim 1 for treating lung repair and lung development disorders.

8) A method according to Claim 1 for treating prostate cancer.

20 9) A method according to Claim 1 for treating pancreatic cancer.

10) A method according to Claim 1 for treating hepatic porphyria.

25 11) A method according to Claim 1 for treating visceral pain.

12) A method according to Claim 1 for treating gastrointestinal secretory disturbances.

13) A method according to Claim 12 for treating duodenal ulcer or *Helicobacter pylori* 30 infection.

14) A method according to Claim 1 for treating emesis or anorexia.

15) A method according to Claim 14 for treating subjects receiving anticancer agents.

16) A method according to Claim 1 for treating inflammatory pain, neuropathic pain,
5 cancer pain, postoperative pain, trigeminal neuralgia pain, acute herpetic pain and post
herpetic pain.

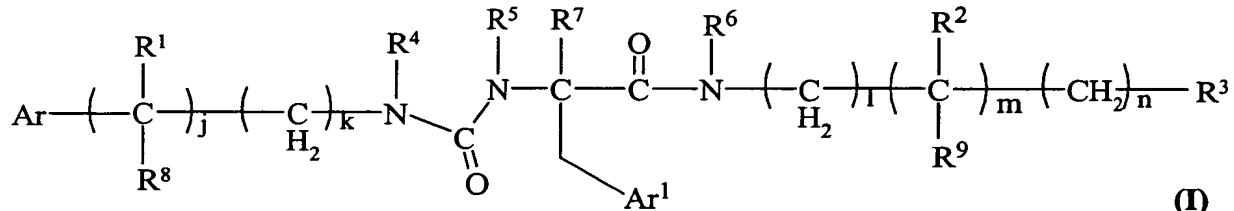
17) A method according to Claim 1 employing (S) 3-(1H-indol-3-yl)-N-[1-(5-methoxy-
pyridin-2-yl)-cyclohexylmethyl]-2-methyl-2-[3-(4-nitro-phenyl)-ureido]-propionamide.

10

18) A method for preventing:

15 sexual dysfunctions, anxiety and panic disorders, social phobia, pulmonary hypertension, lung repair and lung development disorders, prostate cancer, pancreatic cancer, hepatic porphyria, visceral pain, gastrointestinal secretory disturbances, emesis or anorexia, inflammatory pain, neuropathic pain, cancer pain, postoperative pain, trigeminal neuralgia pain, acute herpetic pain and post herpetic pain,

comprising administering to a subject at risk thereof and in need of prophylaxis an effective amount of a compound of Formula I



20 or a pharmaceutically acceptable salt thereof wherein

j is 0 or 1;

k is 0 or 1;

l is 0, 1, 2, or 3;

25

m is 0 or 1;

n is 0, 1 or 2;

Ar is phenyl, pyridyl or pyrimidyl, each unsubstituted or substituted by from 1 to 3 substituents selected from alkyl, halogen, alkoxy, acetyl, nitro, amino, -CH₂NR¹⁰R¹¹, cyano, -CF₃, -NHCONH₂, and -CO₂R¹²;

R^1 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms;

R^8 is hydrogen or forms a ring with R^1 of from 3 to 7 carbon atoms;

R^2 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 8 carbon atoms which can also contain 1 to 2 oxygen or nitrogen atoms;

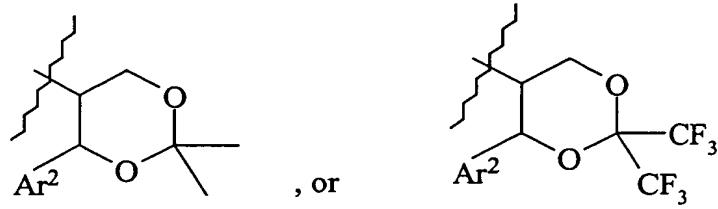
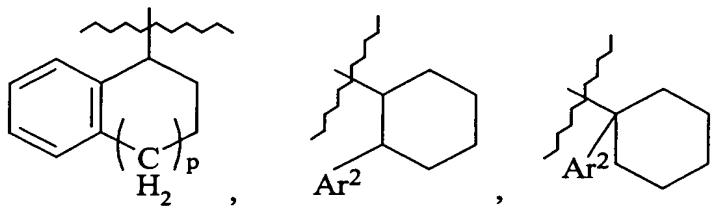
5 R^9 is hydrogen or forms a ring of from 3 to 7 carbon atoms with R^2 which can contain an oxygen or nitrogen atom; or R^2 and R^9 can together be a carbonyl;

Ar^1 can be independently selected from Ar and can also include pyridyl-N-oxide, indolyl, imidazolyl, and pyridyl;

R^4 , R^5 , R^6 , and R^7 are each independently selected from hydrogen and lower alkyl;

10 R^4 can also form with R^5 a covalent link of 2 to 3 atoms which may include an oxygen or a nitrogen atom;

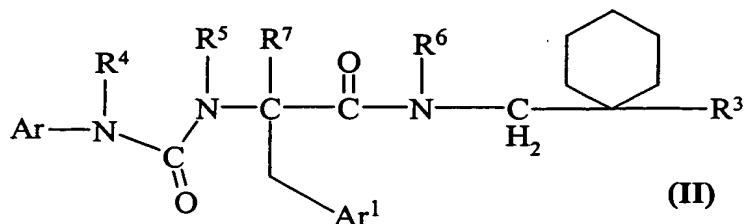
R^3 can be independently selected from Ar or is hydrogen, hydroxy, $-NMe_2$, N-methyl-pyrrolyl, imidazolyl, N-methyl-imidazolyl, tetrazolyl, N-methyl-tetrazolyl, thiazolyl, $-CONR^{13}R^{14}$, alkoxy,



15 , or , wherein p is 0, 1 or 2 and Ar^2 is phenyl or pyridyl;

R^{10} , R^{11} , R^{12} , R^{13} and R^{14} are each independently selected from hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms.

20 19) A method according to Claim 18 employing a compound of Formula II



wherein

Ar is phenyl unsubstituted or substituted with 1 or 2 substituents selected from isopropyl, halo, nitro, and cyano;

5 R⁴, R⁵, and R⁶ are hydrogen;

R⁷ is methyl or hydrogen;

R³ is 2-pyridyl or hydroxy; and

Ar¹ is indolyl, pyridyl, pyridyl-N-oxide, or imidazolyl.

10 20) A method according to Claim 18 for preventing female sexual dysfunctions.

21) A method according to Claim 18 for preventing male sexual dysfunctions.

22) A method according to Claim 18 for preventing anxiety, panic disorders or social

15 phobia.

23) A method according to Claim 18 for preventing pulmonary hypertension.

24) A method according to Claim 18 for preventing lung repair and lung development
20 disorders.

25) A method according to Claim 18 for preventing hepatic porphyria.

26) A method according to Claim 18 for preventing visceral pain.

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27) A method according to Claim 18 for preventing gastrointestinal secretory disturbances.

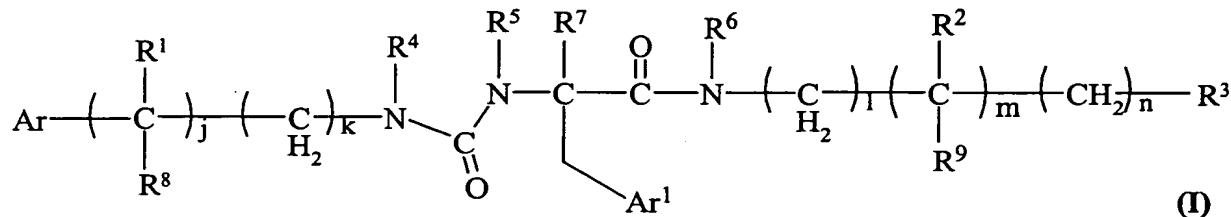
28) A method according to Claim 18 for preventing emesis or anorexia.

29) A method according to Claim 18 for preventing inflammatory pain, neuropathic pain, cancer pain, postoperative pain, trigeminal neuralgia pain, acute herpetic pain and post herpetic pain.

5

30) A method according to Claim 18 employing (S) 3-(1H-indol-3-yl)-N-[1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl]-2-methyl-2-[3-(4-nitro-phenyl)-ureido]-propionamide.

31) A method for diagnosing a mammal for the presence of a mammalian tumour which 10 comprises administering to a mammal a diagnostic imaging amount of a compound of Formula I



or a pharmaceutically acceptable salt thereof wherein

j is 0 or 1;

15 k is 0 or 1;

l is 0, 1, 2, or 3;

m is 0 or 1;

n is 0, 1 or 2;

Ar is phenyl, pyridyl or pyrimidyl, each unsubstituted or substituted by from 1 to 3

20 substituents selected from alkyl, halogen, alkoxy, acetyl, nitro, amino, -CH₂NR¹⁰R¹¹, cyano, -CF₃, -NHCONH₂, and -CO₂R¹²;

R¹ is hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms;

R⁸ is hydrogen or forms a ring with R¹ of from 3 to 7 carbon atoms;

R² is hydrogen or straight, branched, or cyclic alkyl of from 1 to 8 carbon atoms

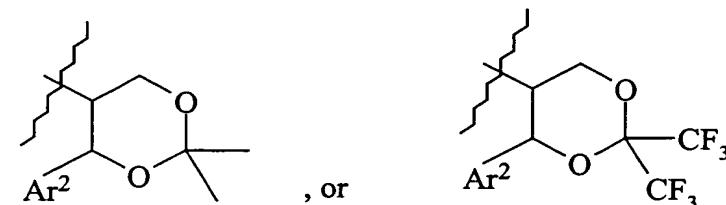
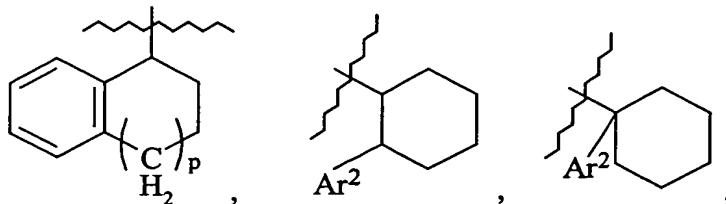
25 which can also contain 1 to 2 oxygen or nitrogen atoms;

R⁹ is hydrogen or forms a ring of from 3 to 7 carbon atoms with R² which can contain an oxygen or nitrogen atom; or R² and R⁹ can together be a carbonyl;

Ar¹ can be independently selected from Ar and can also include pyridyl-N-oxide, indolyl, imidazolyl, and pyridyl;

R^4 , R^5 , R^6 , and R^7 are each independently selected from hydrogen and lower alkyl; R^4 can also form with R^5 a covalent link of 2 to 3 atoms which may include an oxygen or a nitrogen atom;

5 R^3 can be independently selected from Ar or is hydrogen, hydroxy, $-NMe_2$, N -methyl-pyrrolyl, imidazolyl, N -methyl-imidazolyl, tetrazolyl, N -methyl-tetrazolyl, thiazolyl, $-CONR^{13}R^{14}$, alkoxy,



, or , wherein p is 0, 1 or 2 and Ar^2 is phenyl or pyridyl;

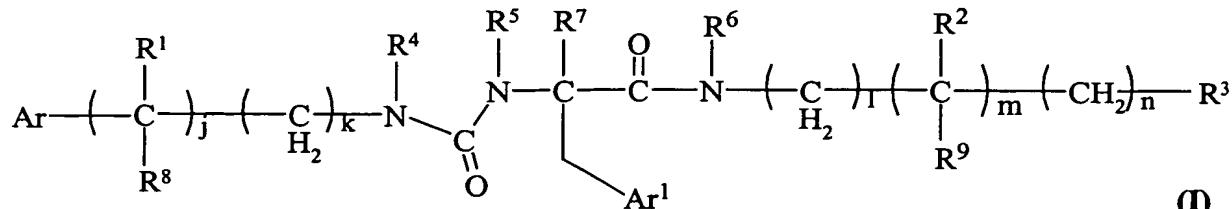
R^{10} , R^{11} , R^{12} , R^{13} and R^{14} are each independently selected from hydrogen

10 or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms.

32) The method of Claim 31 wherein Ar is phenyl substituted with a γ -emitting radionuclide halogen.

15 33) The method of Claim 31 wherein Ar is phenyl substituted with ^{123}I , ^{124}I , ^{125}I , ^{131}I , ^{18}F , ^{76}Br , or ^{77}Br .

34) A method for treating a mammalian tumour which comprises administering to a mammal a composition comprising a tumour-inhibiting amount of a compound of Formula I



or a pharmaceutically acceptable salt thereof wherein

j is 0 or 1;

k is 0 or 1;

l is 0, 1, 2, or 3;

5 m is 0 or 1;

n is 0, 1 or 2;

Ar is phenyl, pyridyl or pyrimidyl, each unsubstituted or substituted by from 1 to 3 substituents selected from alkyl, halogen, alkoxy, acetyl, nitro, amino, -CH₂NR¹⁰R¹¹, cyano, -CF₃, -NHCONH₂, and -CO₂R¹²;

10 R¹ is hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms;

R⁸ is hydrogen or forms a ring with R¹ of from 3 to 7 carbon atoms;

R² is hydrogen or straight, branched, or cyclic alkyl of from 1 to 8 carbon atoms which can also contain 1 to 2 oxygen or nitrogen atoms;

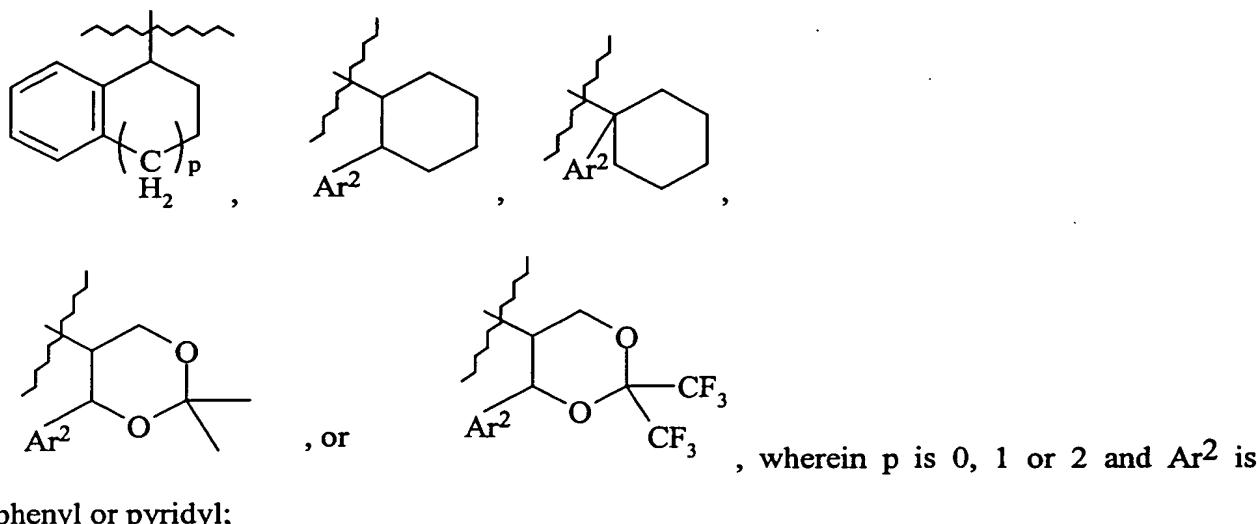
15 R⁹ is hydrogen or forms a ring of from 3 to 7 carbon atoms with R² which can contain an oxygen or nitrogen atom; or R² and R⁹ can together be a carbonyl;

Ar¹ can be independently selected from Ar and can also include pyridyl-N-oxide, indolyl, imidazolyl, and pyridyl;

R⁴, R⁵, R⁶, and R⁷ are each independently selected from hydrogen and lower alkyl;

R⁴ can also form with R⁵ a covalent link of 2 to 3 atoms which may include an oxygen or a nitrogen atom;

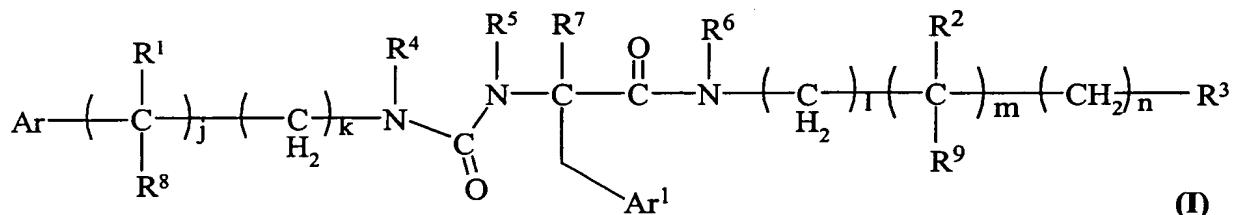
20 R³ can be independently selected from Ar or is hydrogen, hydroxy, -NMe₂, N-methyl-pyrrolyl, imidazolyl, N-methyl-imidazolyl, tetrazolyl, N-methyl-tetrazolyl, thiazolyl, -CONR¹³R¹⁴, alkoxy,



R¹⁰, R¹¹, R¹², R¹³ and R¹⁴ are each independently selected from hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms.

5

35) A method for treating a mammalian tumour which comprises administering to a mammal a composition comprising a tumour-inhibiting amount of a conjugate of a cytotoxic agent with a compound of Formula I



10 or a pharmaceutically acceptable salt thereof wherein

j is 0 or 1;

k is 0 or 1;

l is 0, 1, 2, or 3;

m is 0 or 1;

15 n is 0, 1 or 2;

Ar is phenyl, pyridyl or pyrimidyl, each unsubstituted or substituted by from 1 to 3 substituents selected from alkyl, halogen, alkoxy, acetyl, nitro, amino, -CH₂NR¹⁰R¹¹, cyano, -CF₃, -NHCONH₂, and -CO₂R¹²;

R¹ is hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms;

20 R⁸ is hydrogen or forms a ring with R¹ of from 3 to 7 carbon atoms;

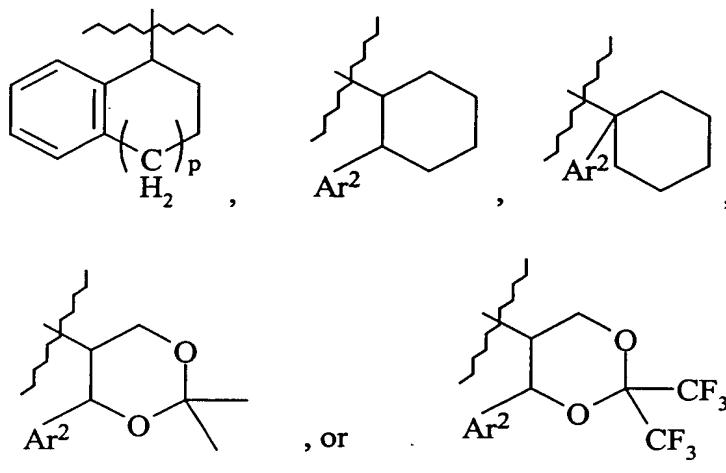
R^2 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 8 carbon atoms which can also contain 1 to 2 oxygen or nitrogen atoms;

R^9 is hydrogen or forms a ring of from 3 to 7 carbon atoms with R^2 which can contain an oxygen or nitrogen atom; or R^2 and R^9 can together be a carbonyl;

5 Ar¹ can be independently selected from Ar and can also include pyridyl-N-oxide, indolyl, imidazolyl, and pyridyl;

R^4 , R^5 , R^6 , and R^7 are each independently selected from hydrogen and lower alkyl; R^4 can also form with R^5 a covalent link of 2 to 3 atoms which may include an oxygen or a nitrogen atom;

10 R^3 can be independently selected from Ar or is hydrogen, hydroxy, $-NMe_2$, N -methyl-pyrrolyl, imidazolyl, N -methyl-imidazolyl, tetrazolyl, N -methyl-tetrazolyl, thiazolyl, $-CONR^{13}R^{14}$, alkoxy,



phenyl or pyridyl;

15 R¹⁰, R¹¹, R¹², R¹³ and R¹⁴ are each independently selected from hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms.

36) The method of Claim 35 wherein the conjugate is cleaved to release the cytotoxic agent on entry into the tumour cells.

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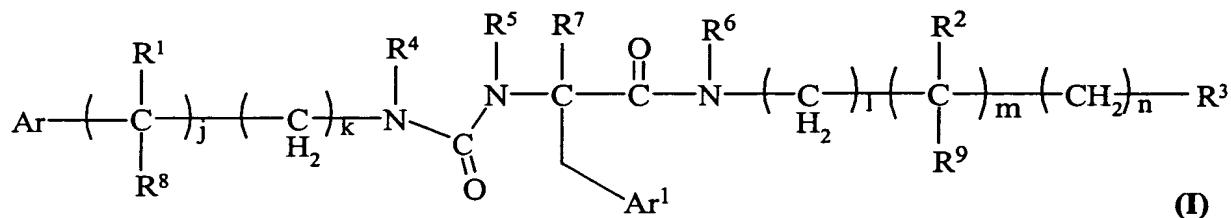
37) The method of Claim 34 wherein Ar is phenyl substituted with a β -emitting or an α -emitting radionuclide halogen.

38) The method of Claim 34 wherein Ar is phenyl substituted with ^{131}I , ^{211}At , ^{76}Br , or ^{77}Br .

39) The method of Claim 31 or 34 wherein said tumour is a pancreatic cancer or a prostate cancer.

40) The method of Claim 31 or 34 wherein said tumour comprises cancer cells which have a cell surface bombesin receptor.

10 41) A method for *in vitro* detection of a cancer cell in a mammalian tissue sample which includes contacting a mammalian tissue sample with an *in vitro* diagnostic amount of a compound of Formula I



or a pharmaceutically acceptable salt thereof wherein

15 j is 0 or 1;

k is 0 or 1;

l is 0, 1, 2, or 3;

m is 0 or 1;

n is 0, 1 or 2;

20 Ar is phenyl, pyridyl or pyrimidyl, each unsubstituted or substituted by from 1 to 3 substituents selected from alkyl, halogen, alkoxy, acetyl, nitro, amino, $-\text{CH}_2\text{NR}^{10}\text{R}^{11}$, cyano, $-\text{CF}_3$, $-\text{NHCONH}_2$, and $-\text{CO}_2\text{R}^{12}$;

R^1 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms;

R^8 is hydrogen or forms a ring with R^1 of from 3 to 7 carbon atoms;

25 R^2 is hydrogen or straight, branched, or cyclic alkyl of from 1 to 8 carbon atoms which can also contain 1 to 2 oxygen or nitrogen atoms;

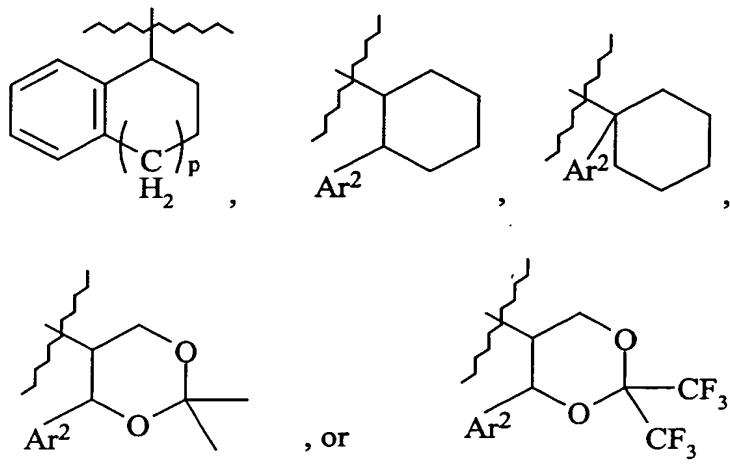
R^9 is hydrogen or forms a ring of from 3 to 7 carbon atoms with R^2 which can contain an oxygen or nitrogen atom; or R^2 and R^9 can together be a carbonyl;

Ar¹ can be independently selected from Ar and can also include pyridyl-N-oxide, indolyl, imidazolyl, and pyridyl;

R⁴, R⁵, R⁶, and R⁷ are each independently selected from hydrogen and lower alkyl;

R⁴ can also form with R⁵ a covalent link of 2 to 3 atoms which may include an oxygen or a 5 nitrogen atom;

R³ can be independently selected from Ar or is hydrogen, hydroxy, -NMe₂, N-methyl-pyrrolyl, imidazolyl, N-methyl-imidazolyl, tetrazolyl, N-methyl-tetrazolyl, thiazolyl, -CONR¹³R¹⁴, alkoxy,



10 phenyl or pyridyl;

R¹⁰, R¹¹, R¹², R¹³ and R¹⁴ are each independently selected from hydrogen or straight, branched, or cyclic alkyl of from 1 to 7 carbon atoms.

42) The method of Claim 41 wherein said cancer cell has a cell surface bombesin receptor.